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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/148,012	09/04/1998	MONTY KRIEGER	MIT7150CIP(2	2616

23579 7590 03/09/2007

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361

EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
2 MONTHS	03/09/2007	PAPER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20070301

Application Number: 09/148,012
Filing Date: September 04, 1998
Appellant(s): KRIEGER, MONTY

Patrea Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 5/15/06.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final rejection filed on 1/17/06 has been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: claims 10 has been canceled.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-9, 12, 15, 16 and 20-22 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The statement of the status of the claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows: Claim 19 is withdrawn from consideration as not directed to the elected invention.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1-9, 12, 15, 16 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was

filed, had possession of the claimed invention. Claim 1, from which all of these rejected claims ultimately depend, recites a method for inhibiting pregnancy or decreasing steroid production by administering a compound altering SR-BI levels in a mammal.

These are genus claims. The claims a drawn to methods which potentially use a universe of compounds. However, Appellant has only provided written description of a small number of specific compounds which act via SR-BI, including estrogen (Example 3 on pages 39-40 of the specification), adenoviral vector encoding SR-BI (Example 5 on pages 40-45 of the specification), and anti-SR-BI antibody (Example 8 on pages 55-66 of the specification) to alter cholesterol levels. Furthermore, Appellant has only described that knocking out the SR-BI gene produces sterile (i.e. altered fertility) transgenic female mice (Example 6, pages 45-54 of the specification).

Furthermore, claims 1-7, 15, 16 and 20-22 recite, or read on, altering SR-BI receptors, or affecting receptor binding to lipoproteins, in *any* tissue. Appellant has not provided adequate written description of which specific tissues modulation of SR-BI would be required in order to inhibit pregnancy. Appellant has only demonstrated that completely knocking out the SR-BI gene (i.e. from all tissues) causes female mice to be infertile (Example 6). In Examples 3 and 4, Applicants have only shown that estrogen-treated rats show an upregulation of SR-BI in adrenal membranes (page 39, line 30 – page 40, line 1) and ovaries (page 40, lines 20-23). Appellants have also demonstrated the effect of hepatic SR-BI overexpression on plasma cholesterol levels (Example 4, especially page 41, lines 12-14 and Table 1). Though compounds which alter steroid levels may be known in the art, again, no nexus between SR-BI expression in these tissues and the ability to inhibit pregnancy has been described.

Additionally, Appellant has not recited the appropriate dosages of any compounds to inhibit pregnancy, nor have they described to what extent SR-BI needs to be altered in the mammal to effectively inhibit pregnancy. There is also no written description as to what length of time these compounds would need to be administered in order to inhibit pregnancy.

Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

Claims 1-9, 15, 16 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, lack of enablement, because the specification, while being enabling for altering cholesterol levels in female mice by knocking out the SR-BI gene, does not reasonably provide enablement for any method of decreasing production of steroids or inhibiting pregnancy in a mammal. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive. Claim 1, from which all claims in the present application ultimately depend, recites a method of inhibiting pregnancy or decreasing steroid production in a mammal by affecting SR-BI. Even, arguendo, Appellant has demonstrated that steroid-lowering compounds were known at the time of the invention, Appellant has provided no guidance and working examples of any compounds which act via SR-BI to alter pregnancy other than those in knockout infertile female mice. In fact, in the specification, estrogen (Example 3 on pages 39-40 of the specification), adenoviral vector encoding SR-BI (Example 5 on pages 40-45 of the specification), and anti-SR-BI antibody (Example 8 on pages 55-66 of the specification) have only been shown to affect SR-BI and to alter cholesterol and lipoprotein levels, but have not been shown to inhibit pregnancy in a mammal. The only method of affecting pregnancy in a mammal that has been demonstrated by the present invention is that showing that SR-BI knockout transgenic female mice are infertile (Example 6, pages 45-54 of the specification). However, a method of knocking out a gene in an embryonic stem cell is not comparable to a method of altering fertility or treating a reproductive disorder in a developed mammal.

The instant fact pattern is similar to that in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor.

Furthermore, the claims of the present invention recite, or read on, altering SR-BI receptors in *any* tissue. Applicant has provided no guidance or working examples of which specific tissues modulation of SR-BI would be required in order to alter pregnancy. Again, Appellant has only demonstrated that completely knocking out the SR-BI gene (i.e. from all tissues) causes female mice to be infertile (Example 6). In Examples 3 and 4, Appellant has only shown that estrogen-treated rats show an

upregulation of SR-BI in adrenal membranes (page 39, line 30 – page 40, line 1) and ovaries (page 40, lines 20-23). Appellant has also demonstrated the effect of hepatic SR-BI overexpression on plasma cholesterol levels (Example 4, especially page 41, lines 12-14 and Table 1). However, no nexus between SR-BI expression in these tissues and the ability to alter pregnancy has been made. It would also be unpredictable to one of ordinary skill in the art how to inhibit pregnancy simply by altering lipoprotein, HDL, LDL, or cholesterol levels in a mammal.

In summary, the breadth of the claims is excessive regarding a method for inhibiting pregnancy comprising administering *any* compound altering SR-BI in the mammal in *any* specific tissue. Appellant has only provided guidance and working examples demonstrating that a complete knockout of the SR-BI gene alters fertility in female mice. These factors, in addition to the lack of predictability as to which compounds affecting steroid levels will inhibit pregnancy, lead the Examiner to hold that undue experimentation is necessary to practice the claimed invention.

(11) Response to Argument

Claim Rejections - 35 USC § 112, first paragraph – written description

In the Appeal Brief filed 5/15/06, Appellant argues that they are the first to recognize that lipoprotein and/or cholesterol levels affect a female's ability to reproduce and that by using SR-BI knockout mice, the SR-BI receptor plays a role in this ability. Appellant has also demonstrated that cholesterol-lowering drugs restore fertility. Appellant further argues that multiple compounds have been identified which lower cholesterol (page 5 of the Brief) and provide Examples 5-8 which demonstrate the effect of SR-BI or SR-BI antibodies on cholesterol levels.

First, the Examiner is confused. In the second paragraph on page 5 of the Brief, Appellant states that increased SR-BI expression *decreases* cholesterol levels. However, in the paragraph bridging pages 5-6, it appears that an increase in SR-BI level *increases* cholesterol levels.

Second, regarding Appellant's claim that multiple classes of compounds are known which affect SR-BI, the claims are still drawn to a universe of compounds while the specification only demonstrates a few means of decreasing steroid production or potentially inhibiting pregnancy in a mammal. These means include estrogen (Example 3 on pages 39-40 of the specification), adenoviral vector encoding SR-BI (Example 5 on pages 40-45 of the specification), and anti-SR-BI antibody (Example 8 on pages 55-66

of the specification). Appellant has not demonstrated any other compounds which alter steroid levels or potentially inhibit pregnancy.

Appellants argue that the disclosure of estrogen, a vector encoding SR-BI and an anti-SR-BI antibody provide broad support for a genus claim. However, though these three means of altering cholesterol are encompassed by the desired genus, they, alone, do not provide adequate written description for the entire genus of compounds able to alter steroid production or pregnancy. In addition, Appellant, respectfully, has argued numerous times that estrogen is not encompassed by the claimed invention. Even, arguendo, these compounds may be known to decrease steroid production in a mammal, they have not been shown to inhibit pregnancy.

Regarding Appellant's argument that he has disclosed an extensive list of molecules on page 11 of the specification which inhibit SR-BI, including molecules which bind SR-BI and compounds which block binding of HDL to SR-BI, it is these groups of compounds which lack the greatest written description. Appellants have only identified estrogen as belonging to one of these classes. Based on this, Appellant is claiming methods using any molecules which bind SR-BI and compounds which decrease steroid production or inhibit pregnancy. Though Appellant is claiming methods, and not the compounds themselves, Appellant still has not provided any written description of these compounds, or any effective amounts to inhibit pregnancy, nor has Appellant shown that any of these compounds, or antibodies, or nucleic acids, are effective in this method. Again, Appellant has only described that knocking out the SR-BI gene produces sterile (i.e. altered fertility) transgenic female mice (Example 6, pages 45-54 of the specification). Appellant has only demonstrated that completely knocking out the SR-BI gene (i.e. from all tissues) causes female mice to be infertile (Example 6). However, in the other examples in the specification, Appellant does not describe how altering SR-BI levels in these tissues alone affects pregnancy, or if altering SR-BI levels *at all* in these tissues is sufficient to inhibit pregnancy. Therefore, though Appellant has taught a method of screening for compounds which alter fertility/pregnancy, as well as a method of drug design, these are general concepts, as no compounds have been described which can be used in the claimed invention. The teachings of Miettinen et al. have previously been considered and, though a link between cholesterol and fertility may have been established, the present specification still does not adequately describe compounds which perform the claimed function.

In addition, Appellant argues that the claimed invention is based on the clear-cut description of the nexus between fertility and cholesterol levels. He argues that since the specification is replete with support for this novel connection the Appellant is entitled to claim all compounds that alter lipoprotein, LDL, HDL, or cholesterol levels for the purpose of altering fertility or treating a reproductive disorder in

a female mammal. Appellant argues that antibodies raised against a portion of the extracellular domain of SR-BI protein inhibit selective uptake of HDL in cultured adrenal cells (Example 8 of the specification) and that adenoviral vectors encoding SR-BI alter cholesterol levels (Example 5). Therefore, the specification discloses specific compounds which alter cholesterol levels. Again, Example 6, as discussed on page 9 of the Brief, discusses embryonic stem cells, not fully formed mammals.

Appellant argues that Examples 3, 5 and 8 have shown a reduction to practice compounds which alter cholesterol. This argument has been considered, but is not deemed persuasive. Again, Applicant is claiming a method of altering pregnancy by altering cholesterol levels. Even, arguendo, this is true, as previously stated, knocking out the SR-BI gene in an embryonic stem cell does not demonstrate the ability to alter pregnancy in a fully formed mammal by administering a compound which alters lipoprotein, LDL, HDL, or cholesterol levels, regardless of whether or not these compounds are acting through SR-BI. These examples only show that Appellant was in possession of compounds which alter cholesterol levels, not which alter pregnancy. Therefore, though Appellant may be correct in stating that "one of ordinary skill in the art will readily recognize not only the direct correlation that exists between cholesterol/HDL and the existence of SR-BI, but also the many compounds that already exist for regulating cholesterol levels," Appellant, respectfully, has only demonstrated just that. He has not demonstrated that he is able to perform the claimed methods, but only the relationship between cholesterol and SR-BI. This can further be seen by comparing claims 4 and 5 as well as 6 and 7. Claims 4 and 6 recite decreasing SR-BI levels, whereas claims 5 and 7 recite increasing SR-BI levels. Therefore, it is not understood how Appellant has adequately supported the present invention when the claims recite either an increase or decrease in SR-BI levels. This adds further support that Appellant wase not in possession of the claimed invention since it is not known in which direction SR-BI must be altered in order to inhibit pregnancy.

While it is true, as argued by Appellant on page 10 of the Brief, that written description does not require that the Appellant reduce to practice all of the claimed species, the Examiner is of the position that NO claimed species other than stem cell knock-outs have been described with regard to inhibiting pregnancy. Appellant further argues on page 10 that "a different degree of description is required where compounds are known and one only needs to provide the criteria for their selection and use." Again, though compounds may have been known which alter steroid levels, they were not known, or have not presently been demonstrated, to inhibit pregnancy, including via SR-BI.

Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

Appellant argues case law on pages 11-12 of the Brief. The Examiner takes no issue with the case law. On pages 12-13 of the Brief, Appellant argues that he was the first to discover a nexus between fertility, steroid levels and cholesterol levels and that, because of this established connection, the Appellant is claiming any compound that alters LDL, HDL or cholesterol mediated by SR-BI.

While these results are interesting, **the infertility in these mice was induced by genetic manipulation of an embryonic stem cell**. There is no evidence of any female reproductive disorder, including in humans, which acts via SR-BI. Appellant has produced a specific genetic alteration in a stem cell to produce this infertility in female mice and have provided no nexus between a method of altering fertility in an SR-BI knockout female mouse and a method of altering fertility in a mammal which is not an SR-BI knockout. *There is no evidence that altering SR-BI levels in a fertile female with normal SR-BI levels and no reproductive disorders will have the desired effect of the claimed method.* Finally, as further evidence for the lack of enablement of the present invention for any method of altering fertility other than to restore fertility in infertile SR-BI knockout female mice, that **there is no evidence in the art that women taking cholesterol-lowering drugs experience any fertility problems, demonstrating that cholesterol-lowering drugs, which would meet the limitation of claim 1, may not alter fertility**.

In considering Appellant's arguments regarding the examples in the specification demonstrating that various compounds bind SR-BI, the Examiner agrees that the specification does disclose various compounds which bind SR-BI, such as estrogen (Example 3 on pages 39-40 of the specification), adenoviral vector encoding SR-BI (Example 5 on pages 40-45 of the specification), and anti-SR-BI antibody (Example 8 on pages 55-66 of the specification). SR-BI knockout transgenic mice have also been shown to produce sterile female mice (Example 6, pages 45-54 of the specification). However, as stated by the Examiner in the previous paragraph, knocking out the SR-BI gene in an embryonic stem cell does not enable the artisan to alter fertility in a fully formed mammal by administering a compound which alters lipoprotein, LDL, HDL, or cholesterol levels, regardless of whether or not these compounds are acting through SR-BI. Therefore, Appellant still has provided no guidance or working examples of compounds which inhibit pregnancy by altering lipoprotein, LDL, HDL, or cholesterol levels in a mammal other than in knockout infertile female mice, regardless of whether or not these compounds act via SR-BI.

Appellant has only demonstrated that they are in possession of compounds which alter cholesterol and that fertility can be restored in transgenic mice lacking the SR-BI gene by administering cholesterol-lowering drugs. This would likely be acceptable if Appellant was claiming a method of increasing fertility

in transgenic mice lacking the SR-BI gene, or methods of altering cholesterol levels by modulating the SR-BI receptor, but this is not the case. Appellant has taken their one example using a transgenic mouse and, respectfully, basically combined it with their in vitro data using antibodies and estrogen to conclude that these cholesterol-lowering drugs can alter fertility in a female mammal. This can further be seen in the claims. Claims 4 and 6 recite decreasing SR-BI levels, whereas claims 5 and 7 recite increasing SR-BI levels. Therefore, it is not understood how Appellant has adequately supported the present invention when the claims recite either an increase or decrease in SR-BI levels. This adds further support for a lack of enablement since Appellants are not able to specify in which direction SR-BI must be altered in order to treat a specific disease, or to alter fertility.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Robert Landsman, Ph.D.
Primary Examiner
Art Unit 1647

Robert Landsman
March 02, 2007

Conferees
Brenda Brumback
Janet Andres

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600